

A Man with Fevers and Chest Pain

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A 42 y/o Hispanic man without significant medical history presented to the ED with the complaint of increasing left-sided chest pain. The patient reported that symptoms began 4 days prior, when he developed a severe headache. That night, he noted increasing chills and sweats, with a fever measured at 103 degrees F. The following morning, he developed left-sided chest pain that he described as a pressure exacerbated by movement and breathing. For the next several days, he reported feeling worse with continuous chills and fever spikes up to 105 degrees F, along with increased severity and duration of his chest pain.

The patient mentioned that acetaminophen and over-the-counter analgesics did not relieve his symptoms. With his chest pain, he also noted associated shortness of breath with mild nausea. However, he denied abdominal pain or changes in his bowel habits, and he reported that his weight had been stable. He had never had these symptoms before.

The patient's past medical history was remarkable for a trauma-related leg fracture in 1995 that was repaired by open reduction and internal fixation. He also had oral surgery in 2000 for severe periodontitis and subsequently had to have a full mouth extraction.

He denied alcohol, tobacco or illicit drug use. He was married for 18 years with 2 healthy children. He denied any HIV risk factors. He also did not report any recent travel or exposure to known sick individuals. He worked at a surgical instrument manufacturing plant.

On admission, his vital signs were: blood pressure 99/62, pulse 133, respirations 22, temperature 99.6 degrees F and oxygenation saturation 96% on room air. He appeared to be acutely ill, although alert and cooperative to exam. His pupils were equal and reactive with normal extraocular movements. He had complete maxillary and mandibular dentures and dry mucus membranes. Cardiac exam revealed a normal S1 and S2, regular rate without appreciable murmurs. Notable findings on lung exam were bibasilar rales. His abdomen was benign, and he did not have evidence of rash or lesions.

An electrocardiogram revealed sinus tachycardia with a rate of 127. Chest x-ray showed bilateral interstitial opacities involving middle and lower lung fields suggestive of an atypical infectious process. There was no cardiomegaly, pulmonary edema or pleural effusions. Laboratory data indicated normal chemistries, a white blood cell count of 14.5 with 84% neutrophils, and 4% bands. Platelets were decreased at 47,000. Cardiac markers were all normal. The INR was 1.23 with a PTT of 36.

A presumptive diagnosis of community-acquired versus atypical pneumonia was made and the patient was rehydrated and started on iv moxifloxacin. The night of admission, the patient's clinical status quickly deteriorated with increasing oxygen requirements up to 5 liters via nasal cannula, with oxygen saturations in the low 90% range. Complete blood count drawn the next morning revealed a white blood cell count of 16.1 and platelets at 35,000. Physical exam the next day was noteworthy for a new systolic ejection murmur heard best at the apex with radiation to the axilla. A thorough skin exam revealed characteristic splinter hemorrhages and Janeway lesions on the palmer surface of hands and the soles of the feet (See Figures F and G, Color Plates page 19). A formal fundoscopic exam revealed Roth's spots in both eyes. A transthoracic echocardiogram was done, which showed a 1.6 cm x 1.4 cm mass attached to the lateral base of the posterior leaflet of the mitral valve. The mass was noted to be smooth with no projections. It was felt to be rather unusual and atypical for a vegetation. The ejection fraction was normal. Admission blood cultures came back positive for gram positive cocci in clusters. A DIC panel showed increased D-dimer, decreased fibrinogen and elevated INR.

The clinical picture was most consistent with acute bacterial endocarditis. The patient was started empirically on vancomycin and gentamycin.

He continued to do poorly with higher oxygen requirements to maintain saturations greater than 90%. A portable chest x-ray showed frank pulmonary edema. The patient was urgently transferred to the cardiac care unit with presumed mitral valve failure, secondary to the vegetation. His blood pressures were controlled with nipride and hydralazine and he was aggressively diuresed

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with iv furosemide. The antibiotic regimen was broadened to include Rifampin. Unfortunately, he did not improve clinically. Multiple blood cultures continued to show *Staphylococcus aureus*, despite several days of antibiotic therapy. The decision was made, in consultation with Cardiac Surgery, to take the patient to the operating room for emergent mitral valve replacement. Intraoperatively, a 2 cm x 2 cm friable vegetation was noted at the posterior leaflet of the mitral valve. There was also a large abscess cavity burrowing into the annulus destroying about 2/3 of the posterior annulus. Histopathology revealed *Staph aureus* colonies embedded within the vegetation (See Figures H-J, Color Plates page 19). Postoperatively, the patient did well for the next 48 hours, and was deemed stable for transfer out of the cardiothoracic critical care unit. Shortly thereafter, he again developed temperature spikes, with persistently positive blood cultures despite re-initiation of antibiotics. On post-op day 7, he had an acute episode of shortness of breath with evidence of pulmonary edema, requiring reintubation. It was determined that his prosthetic mitral valve had been reinfected and was failing. Despite all heroic efforts, the patient ultimately succumbed to sepsis.

Discussion

Infective endocarditis (IE) is defined as an infection which can produce vegetations on the endocardium, including valves, septae, or mural endocardium. IE is almost invariably fatal, if untreated. An estimated 10,000 to 15,000 new cases of IE are diagnosed in the USA each year, with male to female ratios ranging from 2:1 to as high as 9:1. IE can be broadly classified into native valve and prosthetic valve infection, with subdivisions within each category based on the microorganism (further classifications can also be made based on the nature of the infected valve; this will be expounded further in treatment options). Although native valve endocarditis can be caused by almost any kind of bacteria, the three most common include streptococci, staphylococci and enterococci. The HACEK organisms (*Haemophilus*, *Actinobacillus*, *Cardiobacterium*, *Eikenella*, and *Kingella*) are oral flora that cause a subacute presentation and are very difficult to grow on media, hence the term 'culture negative' endocarditis. In patients who have indwelling

catheters and/or are immunocompromised, fungal IE can occur with *Candidia* and *Aspergillus* species. Prosthetic valves predispose to endocarditis. In one study, IE of prosthetic valves accounted for 10-20 percent of cases. In addition to valves, intravascular sutures and pacemaker wires can also become foci of infection. Early onset prosthetic valve endocarditis (less than 60 days after surgery) is usually secondary to intraoperative contamination or perioperative bacteremia. Approximately half of all cases are caused by staphylococci, with *S. epidermidis* more frequent than *S.aureus*. Gram negative rods can account for up to 15 percent and fungi up to 10 percent of early cases. When late endocarditis occurs (onset > 60 days) the organism is usually a streptococcus species (about 40% of cases). Early prosthetic IE often runs a fulminant course, with valvular dysfunction and valve dehiscence. Although late prosthetic IE can progress similarly, more often the clinical course resembles non-prosthetic IE with streptococcus and is luckily not as catastrophic. There are several known risk factors for the development of IE, including injection drug use, prosthetic heart valves, and structural heart disease. Other factors have been postulated to increase the risk of IE. These form the theoretical basis for antimicrobial prophylaxis prior to planned invasive procedures in certain individuals. Several criteria have been developed for the diagnosis of IE. It should be noted that the diagnosis is ultimately based on the clinical picture and compulsory adherence to set criteria is usually not necessary. That being said, the Modified Duke Criteria is one of the most commonly used set of guidelines, using a schema of major and minor criteria. Major criteria include positive blood cultures for organisms that cause IE, evidence of endocardial involvement, suggestive echocardiogram findings, and new valvular regurgitation. Minor criteria are many and include: history of intravenous drug use or structural heart disease, fevers >100.4 degrees F, vascular stigmata such as Janeway lesions, or septic emboli, immunologic phenomena such as Osler's nodes or glomerulonephritis, and microbiological evidence. A definite diagnosis is made on either pathological OR clinical criteria. Clinical criteria usually requires 2 major criteria or 1 major and 3 minor or 5 minor criteria. Possible IE is defined as 1 major and 1 minor OR 3 minor.

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The treatment of IE is dependent on the valve, as well as the suspected organism. The following table summarizes the different regimens available to treat IE. (Although only one choice is presented, it should be noted that there are alternative antibiotics that can be used for each type of infection.)

Type of Infection	Antibiotic Choice	Length of Treatment
Native Valve IE from PCN sensitive Streptococcus	PCN G 12-18 million U/24hr OR Ceftriaxone 2gm IV q24h	4 weeks
Native Valve IE from PCN resistant Streptococcus	Vancomycin 30mg/kg per 24h IV in 2 divided doses	4 weeks
Standard Therapy for Endocarditis due to Enterococcus	Ampicillin 12g/24h IV WITH Gentamycin 1g/kg IV every 8h	4 – 6 weeks
Native Valve IE due to Methicillin Sensitive Staphylococcus	Nafcillin/Oxacillin 2gm IV every 4h WITH Gentamycin 1mg/kg IV every 8h	4 – 6 weeks
Prosthetic Valve IE with Methicillin Resistant Staphylococcus	Vancomycin 30mg/kg per 24h IV WITH Rifampin 300mg orally every 8h WITH Gentamycin 1mg/kg IV every 8h	Greater than 6 weeks
Prosthetic Valve IE with Methicillin Sensitive Staphylococcus	Nafcillin/Oxacillin 2g IV every 4h WITH Rifampin 300mg orally every 8h WITH Gentamycin 1mg/kg IV every 8h	Greater than 6 weeks
Therapy due to HACEK Microorganism	Ceftriaxone 2g IV every 24h	4 weeks

From Wilson, WR, Karchmer, AW, Dajani, AS, et al, JAMA 1995; 274:1706

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